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L3 24 DUP REMOVE L2 (8 DUPLICATES REMOVED)

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L3 ANSWER 1 OF 24 CAPLUS COPYRIGHT 2004 ACS on STN
2004:41233 Document No. 140:92605 Immune modulatory activity of human ribonucleases. Fu, Qin; Tchernev, Velizar; Satyaraj, Ebenezer; Patel, Dhavalkumar D.; Kingsmore, Stephen F.; Schweitzer, Barry (Molecular Staging, Inc., USA). PCT Int. Appl. WO 2004004668 A2 20040115, 37 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-US8824 20030402. PRIORITY: US 2002-PV393110 20020703; US 2002-PV394511 20020710; US 2003-396317 20030326.

AB Human extracellular RNases are widely distributed in various organs and body fluids and together with other members of the mammalian RNase A superfamily. In addition to their RNase activity, several RNases have been shown to have special biol. actions, i.e., antitumor, antiviral and angiogenic properties. However, the mol. mechanisms of such activities are unclear. Using protein microarrays amplified rolling circle amplification (RCA), the authors investigated the effects of EDN (Rnase 2), ECP (Rnase 3) and RNase 1 on leukocyte cytokine production The authors measured the levels of 78 different cytokines and growth factors in culture supernatants to determine the cytokine profiles of cells treated with different combinations of RNases and RNase inhibitors. Members of human RNase family (such as Rnase 1, hEDN (Rnase 2) and Rnase 3) induced expression of certain sets of cytokines in human leukocytes, including ENA-78, EOT2, BLC, GDNF, I309, IFN-α, IFN-γ, IL-10, IL-12p70,

IL-13, IL-16, IL-18, IL-1β, IL-1ra, soluble IL-2Rα, IL-3, IL-6, soluble IL-6R, IL-7, IL-8, IP-10, MCP-1, MCP-2, MCP-3, MCSF, MIG, MDC, MIP-1α, MIP-1β, MPIF-1, NAP-2, RANTES, soluble CD23, OSM, TARC, TNF-α, TNF-R1 and uPAR. Thus members of the Rnase superfamily are therapeutic targets for treatment of inflammatory diseases and clin. conditions. Inhibition or augmentation of Rnase expression is used to modulate the immune system and is beneficial for host defense against various diseases and is exploited as an adjuvant. The expression of RNases is a diagnostic marker for inflammation related conditions and is used to determine various disease stages. In addition, expression of cytokines, chemokines, growth factors is used to monitor efficacy of Rnase-base therapies.

L3 ANSWER 2 OF 24 CAPLUS COPYRIGHT 2004 ACS on STN

2003:97450 Document No. 138:152268 Concatenation of functional domains on immunoadhesins. Chung, Yong-Hoon; Han, Ji-Woong; Lee, Hye-Ja; Choi, Eun-Yong; Kim, Jin-Mi (Medexgen Co. Ltd., S. Korea). PCT Int. Appl. WO 2003010202 A1 20030206, 211 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-KR1427 20020726. PRIORITY: KR 2001-45028 20010726.

AB The authors disclose concatameric proteins comprising two soluble domains linked in tandem to the Fc fragment of IgG. The disclosed concatameric proteins can form dimers via intermol. disulfide bonds at the hinge region of two monomeric proteins. In one example, the concatameric monomer protein is comprised of two extracellular domains of the p75 tumor necrosis factor receptor fused to the Fc fragment of IgG1. The dimeric fusion protein was shown to inhibit the cytotoxicity of its ligands and to exhibit an ameliorative effect in a rheumatoid arthritis model.

L3 ANSWER 3 OF 24 CAPLUS COPYRIGHT 2004 ACS on STN

2002:927271 Document No. 137:383804 Anti-NGF antibodies for the treatment of various disorders. Shelton, David L. (Genentech, Inc., USA). PCT Int. Appl. WO 2002096458 A1 20021205, 67 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US15284 20020509. PRIORITY: US 2001-PV294392 20010530.

AB The present invention relates generally to methods of using anti-nerve growth factor antibodies in the treatment of various NGF-related disorders, including asthma, multiple sclerosis, arthritis, lupus erythematosus, and psoriasis. The antibodies bind to NGF with high affinity and inhibit the binding of NGF to TrkA. The antibodies can be antibody fragments, chimeric or humanized antibodies, or bispecific antibodies which can also bind to **IgE**, TNF, or TNF receptor. The methods are effective in treating these disorders in a patient without having a significant adverse effect on the immune system of the patient. The antibodies can be used in combination with other therapeutic agents to treat NGF-related disorders.

L3 ANSWER 4 OF 24 CAPLUS COPYRIGHT 2004 ACS on STN

2002:408909 Document No. 136:398188 An extended tethering approach for rapid identification of ligands. Erlanson, Daniel A.; Braisted, Andrew;

McDowell, Robert; Prescott, John (Sunesis Pharmaceuticals, Inc., USA). PCT Int. Appl. WO 2002042773 A2 20020530, 62 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US44036 20011120. PRIORITY: US 2000-PV252294 20001121.

AB The invention concerns a method for rapid identification and characterization of binding partners for a target mol., and for providing binding partners with improved binding affinity. More specifically, the invention concerns an improved tethering method for the rapid identification of at least two binding partners that bind near one another to a target mol. This approach is based on the design of a Small Mol. Extender (SME) that is tethered, via a reversible or irreversible covalent bond, to a Target Mol. (TM) at or near a first site of interest, and has a chemical reactive group reactive with small organic mols. to be screened for affinity to a second site of interest on the TM. Accordingly, the SME is used for screening a plurality of ligand candidates to identify a ligand that has intrinsic binding affinity for a second site of interest on the TM. If desired, further SME's can be designed based on the identification of the ligand with binding affinity for the second site of interest, and the screening can be repeated to identify further ligands having intrinsic binding affinity for the same or other site(s) of interest on the same or related TM's.

L3 ANSWER 5 OF 24 CAPLUS COPYRIGHT 2004 ACS on STN

2002:157624 Document No. 136:215409 Anti-novel **neurotrophic factor** 1 (NNT-1) antibodies and soluble NNT-1 receptor for treating **IgE**-related disease. Senaldi, Giorgio (Amgen Inc., USA). PCT Int. Appl. WO 2002015977 A2 20020228, 63 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US25906 20010817. PRIORITY: US 2000-PV226436 20000818; US 2001-931704 20010816.

AB Disclosed are novel methods and compns. for diagnosing and treating **IgE**-related diseases using NNT-1 inhibitors. The NNT-1 inhibitors include antagonistic anti-NNT-1 antibodies, chimeric or humanized antibodies, and CDR-grafted antibodies or fragments, as well as soluble NNT-1 receptor. The **IgE**-related diseases include allergy, allergic rhinitis, eczema, dermatitis, pollinosis, asthma, and others. In one embodiment, the present invention relates to a method of treating **IgE**-related diseases using a selective binding agent to NNT-1. In another embodiment, the present invention relates to a method of treating **IgE**-related diseases using an NNT-1 expression modulator. Methods of modulating **IgE** levels, and of diagnosing, preventing and/or treating certain types of allergic diseases using NNT-1 inhibitors are also disclosed.

L3 ANSWER 6 OF 24 CAPLUS COPYRIGHT 2004 ACS on STN

2002:123073 Document No. 136:182471 Peptidomimetics containing helix-turn-helix motif and cytokine epitope for preventing cytokine-related diseases. Serrano, Luis; Domingues, Helena Maria (European Molecular Biology Laboratory, Germany). PCT Int. Appl. WO 2002012337 A1 20020214, 43 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE,

KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-IB1705 20010809. PRIORITY: GB 2000-19638 20000809.

AB The invention relates to peptide mimetics of cytokine mols. that comprise an atypical helix-turn-helix motif that has been mutated to incorporate one or more amino acid residues from the active site of said cytokine mol. In particular, the invention relates to peptide mimetics of type I cytokine mols. such as interleukin 4, (IL-4), human growth hormone (HGH) and interleukin 2 (IL-2). Chimeric peptidomimetic solup10 comprising atypical helix-turn-helix motif of ROP protein and IL-4 epitope was prepared and used for treating or preventing diseases associated with immune cell growth and differentiation, helminthic macroparasite infection, tumor and **IgE** induction (i.e. allergic reactions).

L3 ANSWER 7 OF 24 CAPLUS COPYRIGHT 2004 ACS on STN

2002:794210 Document No. 137:275361 Extended tethering approach for rapid identification of ligands. Erlanson, Daniel A.; Braisted, Andrew C.; McDowell, Robert; Prescott, John (USA). U.S. Pat. Appl. Publ. US 2002150947 A1 20021017, 35 pp., Cont.-in-part of U. S. Provisional Ser. No. 310,725. (English). CODEN: USXXCO. APPLICATION: US 2001-990421 20011121. PRIORITY: US 2000-PV252294 20001121; US 2001-PV310725 20010807.

AB The invention concerns a method for rapid identification and characterization of binding partners for a target mol., and for providing binding partners with improved binding affinity. More specifically, the invention concerns an improved tethering method for the rapid identification of at least two binding partners that bind near one another to a target mol. This approach is based on the design of a Small Mol. Extender (SME) that is tethered, via a reversible or irreversible covalent bond, to a Target Mol. (TM) at or near a first site of interest, and has a chemical reactive group reactive with small organic mols. to be screened for affinity to a second site of interest on the TM. Accordingly, the SME is used for screening a plurality of ligand candidates to identify a ligand that has intrinsic binding affinity for a second site of interest on the TM. If desired, further SME's can be designed based on the identification of the ligand with binding affinity for the second site of interest, and the screening can be repeated to identify further ligands having intrinsic binding affinity for the same or other site(s) of interest on the same or related TM's.

L3 ANSWER 8 OF 24 CAPLUS COPYRIGHT 2004 ACS on STN

2002:937303 Document No. 138:20443 Endocrine disruptor screening using DNA chips of endocrine disruptor-responsive genes. Kondo, Akihiro; Takeda, Takeshi; Mizutani, Shigetoshi; Tsujimoto, Yoshimasa; Takashima, Ryokichi; Enoki, Yuki; Kato, Ikunoshin (Takara Bio Inc., Japan). Jpn. Kokai Tokkyo Koho JP 2002355079 A2 20021210, 386 pp. (Japanese). CODEN: JKXXAF. APPLICATION: JP 2002-69354 20020313. PRIORITY: JP 2001-73183 20010314; JP 2001-74993 20010315; JP 2001-102519 20010330.

AB A method and kit for detecting endocrine-disrupting chems. using DNA microarrays are claimed. The method comprises preparing a nucleic acid sample containing mRNAs or cDNAs originating in cells, tissues, or organisms which have been brought into contact with a sample containing the endocrine disruptor. The nucleic acid sample is hybridized with DNA microarrays having genes affected by the endocrine disruptor or DNA fragments originating in these genes have been fixed. The results obtained are then compared with the results obtained with the control sample to select the gene affected by the endocrine disruptor. Genes whose expression is altered by tri-Bu tin, 4-octaphenol, 4-nonylphenol, di-N-Bu phthalate, dichlorohexyl phthalate, octachlorostyrene, benzophenone, diethylhexyl phthalate, diethylstilbestrol (DES), and 17-β estradiol (E2), were found in mice by DNA chip anal.

L3 ANSWER 9 OF 24 CAPLUS COPYRIGHT 2004 ACS on STN
2002:414841 Document No. 137:45807 Regulatory effects of novel neurotrophin-1/B cell-stimulating factor-3 (cardiotrophin-like cytokine) on B cell function. Senaldi, Giorgio; Stolina, Marina; Guo, Jane; Faggioni, Raffaella; McCabe, Susan; Kaufman, Stephen A.; Van, Gwyneth; Xu, Weilong; Fletcher, Frederick A.; Boone, Thomas; Chang, Ming-Shi; Sarmiento, Ulla; Cattley, Russell C. (Amgen, Inc., Thousand Oaks, CA, 91320, USA). Journal of Immunology, 168(11), 5690-5698 (English) 2002. CODEN: JOIMA3. ISSN: 0022-1767. Publisher: American Association of Immunologists.

AB The authors describe regulatory effects that a novel neurotrophin-1/B cell-stimulating factor-3 (NNT-1/BSF-3; also reported as cardiotrophin-like cytokine) has on B cell function. NNT-1/BSF-3 stimulates B cell proliferation and Ig production in vitro. NNT-1/BSF-3-transgenic mice, engineered to express NNT-1/BSF-3 in the liver under control of the apolipoprotein E promoter, show B cell hyperplasia with particular expansion of the mature follicular B cell subset in the spleen and the prominent presence of plasma cells. NNT-1/BSF-3-transgenic mice show high serum levels of IgM, **IgE**, IgG2b, IgG3, anti-dsDNA Abs, and serum amyloid A. NNT-1/BSF-3-transgenic mice also show non-amyloid mesangial deposits that contain IgM, IgG, and C3 and are characterized by a distinctive ultrastructure similar to that of immunotactoid glomerulopathy. NNT-1/BSF-3-transgenic mice produce high amts. of Ag-specific IgM, IgA, and **IgE** and low amts. of IgG2a and IgG3. Normal mice treated with NNT-1/BSF-3 also produce high amts. of Ag-specific **IgE**. NNT-1/BSF-3 regulates immunity by stimulating B cell function and Ab production, with preference for Th2 over Th1 Ig types.

L3 ANSWER 10 OF 24 CAPLUS COPYRIGHT 2004 ACS on STN
2002:683861 Document No. 137:380319 Gene expression profile after intense second messenger activation in cortical primary neurones. Mayer, Peter; Ammon, Susanne; Braun, Holger; Tischmeyer, Helga; Riechert, Uta; Kahl, Evelyn; Hollt, Volker (Institute for Pharmacology and Toxicology, Otto von Guericke University Magdeburg, Magdeburg, D-39120, Germany). Journal of Neurochemistry, 82(5), 1077-1086 (English) 2002. CODEN: JONRA9. ISSN: 0022-3042. Publisher: Blackwell Science Ltd..

AB Numerous stimuli induce immediate early gene (IEG) expression in neurons, but a comprehensive overview of the late-response genes is lacking. Therefore we aimed to identify changes in the neuronal gene expression profile following intense stimulation. Forskolin and 12-O-tetradecanoylphorbol-13-acetate (TPA), direct activators of intracellular second messengers, were applied to primary cultured cortical neurons. The gene expression profiles were analyzed on Affymetrix DNA chips which cover around 8000 rat genes. Out of these, 95 genes (1.2%) were increased at least three-fold, and 43 genes (0.5%) were at least three-fold decreased. The gene chip results were verified by testing 15 of the altered genes by quant. real-time PCR. The majority of the up-regulated genes were transcription factors, **neurotrophic factors** or (putative) neuropeptides. Furthermore, there were marked changes in intracellular signal processing enzymes and in postsynaptic structural proteins (e.g. vesl, arc, narp), which have been implicated in synaptic plasticity. Notably, classical players in neurotransmission or plasticity such as glutamate and GABA receptors or voltage-gated ion channels were not increased. It is likely that the increased production of components of intracellular signaling and of postsynaptic proteins is involved in neuronal plasticity.

L3 ANSWER 11 OF 24 CAPLUS COPYRIGHT 2004 ACS on STN
2001:828415 Document No. 137:89412 Detection of variations in the DNA methylation profile of genes in the determining the risk of disease. Berlin, Kurt; Piepenbrock, Christian; Olek, Alexander (Epigenomics A.-G., Germany). PCT Int. Appl. WO 2001077373 A2 20011018, 636 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD,

MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (German). CODEN: PIXXD2. APPLICATION: WO 2001-XA1486 20010406. PRIORITY: DE 2000-10019058 20000406; WO 2001-DE1486 20010406.

AB The invention relates to an oligonucleotide kit as probe for the detection of relevant variations in the DNA methylation of a target group of genes. The invention further relates to the use of the same for determining the gene variant with regard to DNA methylation, a medical device, using an oligonucleotide kit, a method for determining the methylation state of an individual and a method for the establishment of a model for establishing the probability of onset of a disease state in an individual. Such diseases may be: undesired pharmaceutical side-effects; cancerous diseases; CNS dysfunctions, injuries or diseases; aggressive symptoms or relational disturbances; clin., psychol. and social consequences of brain injury; psychotic disorders and personality disorders; dementia and/or associated syndromes; cardiovascular disease, dysfunction and damage; dysfunction, damage or disease of the gastrointestinal tract; dysfunction, damage or disease of the respiratory system; injury, inflammation, infection, immunity and/or anastasis; dysfunction, damage or disease of the body as an abnormal development process; dysfunction, damage or disease of the skin, muscle, connective tissue or bones; endocrine and metabolic dysfunction, damage or disease; headaches or sexual dysfunction. This abstract record is one of several records for this document necessitated by the large number of index entries required to fully index the document and publication system constraints.

L3 ANSWER 12 OF 24 CAPLUS COPYRIGHT 2004 ACS on STN

2001:50811 Document No. 134:111243 Method for selecting high-expressing host cells using dicistronic expression system containing selectable/amplifiable gene within an intron. Chisholm, Vanessa; Crowley, Craig W.; Krummen, Lynne A.; Meng, Yu-Ju G. (Genentech, Inc., USA). PCT Int. Appl. WO 2001004306 A1 20010118, 75 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US18841 20000711. PRIORITY: US 1999-PV143360 19990712.

AB Vectors and methods for efficient isolation of recombinant cells expressing high levels of a desired protein are provided. The vectors comprise an amplifiable selectable gene, a fluorescent protein gene, and a gene encoding a desired product in a manner that optimizes transcriptional and translational linkage. The method utilizes eukaryotic host cells harboring a DNA construct comprising a selectable gene (preferably an amplifiable gene) and a product gene provided 3' to the selectable gene. The selectable gene is positioned within an intron defined by a splice donor site and a splice acceptor site and the selectable gene and product gene are under the transcriptional control of a single transcriptional regulatory region. The splice donor site is generally an efficient splice donor site and thereby regulates expression of the product gene using the transcriptional regulatory region. The transfected cells are cultured so as to express the gene encoding the product in a selective medium comprising an amplifying agent for sufficient time to allow amplification to occur, whereupon either the desired product is recovered or cells having multiple copies of the product gene are identified. CHO cells containing tissue plasminogen activator (tPA) expression vectors according to the invention produced ≥9-fold higher tPA levels after amplification than did CHO cells containing conventional vectors. The vector was a pRK derivative This vector contains a cytomegalovirus immediate early promoter and an intron having a splice donor site derived from the

cytomegalovirus immediate early gene and a splice acceptor site from an IgG heavy chain variable region gene. The DHFR gene was inserted into this intron and the tPA gene was inserted downstream of the splice acceptor site.

L3 ANSWER 13 OF 24 CAPLUS COPYRIGHT 2004 ACS on STN
2001:755465 Document No. 136:278038 Nerve growth factor or IL-3 induces more IL-13 production from basophils of allergic subjects than from basophils of nonallergic subjects. Sin, Aytul Z.; Roche, Ellen M.; Togias, Alkis; Lichtenstein, Lawrence M.; Schroeder, John T. (Department of Medicine, Johns Hopkins Asthma & Allergy Center, Baltimore, MD, 21224, USA). Journal of Allergy and Clinical Immunology, 108(3), 387-393 (English) 2001. CODEN: JACIBY. ISSN: 0091-6749. Publisher: Mosby, Inc..
AB Studies show that nerve growth factor (NGF) exhibits immunomodulatory activity. This neurotrophin is found at high levels in the serum of asthmatic individuals, is released during allergic reactions, and is reported to augment in vitro histamine and leukotriene C4 release by human basophils. Because basophils represent a substantial source of IL-4 and IL-13, the authors tested the effects of NGF on the secretion of these cytokines by cells prepared from allergic subjects and cells prepared from nonallergic subjects. Cytokine and histamine were measured in culture supernatants by ELISA and fluorometry, resp. Both real-time RT-PCR and conventional RT-PCR were used to measure IL-13 mRNA expression. NGF receptor expression was determined by 2-color flow cytometry. Basophil suspensions from allergic subjects secreted some 2.5-fold greater levels of IL-13 when cultured with NGF than did cells prepared from normal control subjects. Flow cytometry revealed no differences in TrkA receptors on basophils to explain these findings. The levels of IL-13 secreted by the 2 groups of donors also differed when cells were activated with IL-3 but not when they were activated with anti-**IgE** antibody. Both NGF and IL-3 failed to induce IL-13 in cell cultures depleted of basophils, suggesting that the measurable IL-13 was indeed basophil-derived. Real-time RT-PCR showed an average induction of IL-13 message above medium control that was 4.3-fold with NGF and 8.9-fold with IL-3. Finally, NGF priming resulted in a remarkable enhancement of IL-13 induced by anti-**IgE**. This was greater than the priming observed for either the IL-4 or histamine when this stimulus was used. Thus, NGF (like IL-3) can both directly stimulate IL-13 secretion and modulate **IgE**-mediated responses in basophils. Its enhanced effect on cells from allergic individuals raises the importance of this cytokine in the pathogenesis of allergic disease.

L3 ANSWER 14 OF 24 CAPLUS COPYRIGHT 2004 ACS on STN
2001:413140 Document No. 135:150846 EGR2 mutations in inherited neuropathies dominant-negatively inhibit myelin gene expression. Nagarajan, Rakesh; Svaren, John; Le, Nam; Araki, Toshiyuki; Watson, Mark; Milbrandt, Jeffrey (Departments of Pathology and Internal Medicine, Washington University School of Medicine, St. Louis, MO, 63110, USA). Neuron, 30(2), 355-368 (English) 2001. CODEN: NERNET. ISSN: 0896-6273. Publisher: Cell Press.
AB The identification of EGR2 mutations in patients with neuropathies and the phenotype Egr2/Krox20-/- have demonstrated that the Egr2 transcription factor is critical for peripheral nerve myelination. However, the mechanism by which these mutations cause disease remains unclear, as most patients present with disease in the heterozygous state, whereas Egr2+/- mice are phenotypically normal. To understand the effect of aberrant Egr2 activity on Schwann cell gene expression, we performed microarray expression profiling to identify genes regulated by Egr2 in Schwann cells. These include genes encoding myelin proteins and enzymes required for synthesis of normal myelin lipids. Using these newly identified targets, we have shown that neuropathy-associated EGR2 mutants dominant-neg. inhibit wild-type Egr2-mediated expression of essential myelin genes to levels sufficiently low to result in the abnormal myelination observed in these patients.

L3 ANSWER 15 OF 24 MEDLINE on STN DUPLICATE 1
2002002004 Document Number: 21621794. PubMed ID: 11750074. Mast cells

differentially express and release active high molecular weight neurotrophins. Skaper S D; Pollock M; Facci L. (Neurology Centre of Excellence for Drug Discovery, GlaxoSmithKline Pharmaceuticals, New Frontiers Science Park, Third Avenue, Harlow, Essex CM19 5AW, UK.. stephen_skaper-1@gsk.com) . BRAIN RESEARCH. MOLECULAR BRAIN RESEARCH, (2001 Dec 30) 97 (2) 177-85. Journal code: 8908640. ISSN: 0169-328X. Pub. country: Netherlands. Language: English.

AB Nerve growth factor (NGF), a target-derived factor for survival and maintenance of peripheral and central neurons, has been implicated in inflammatory processes. Mast cells are the principal effector cells in **IgE**-dependent hypersensitivity reactions, and also play a role in diseases characterised by inflammation, including those of the nervous system like multiple sclerosis. Mast cells are capable of synthesising and responding to NGF, although the occurrence of other members of the NGF family of neurotrophins and their protein forms have not been described. Immunoblot analysis with highly selective neurotrophin antibodies has now been used to show that rat peritoneal mast cells express a higher molecular weight form (73 kDa) of NGF, but not the monomeric (13 kDa) NGF polypeptide. Mast cells also expressed 73 kDa forms of neurotrophin-4 and neurotrophin-3; brain-derived **neurotrophic factor** was not detected. Medium conditioned by degranulating peritoneal mast cells contained similar high molecular weight forms of NGF and neurotrophin-4 on Western blots, but no neurotrophin-3. Mast cell-derived neurotrophin immunoreactivities were inhibited by the respective peptide antigen, further demonstrating the specificity of the mast cell-derived neurotrophic protein. Mast cell-released proteins supported the survival of cultured chicken embryonic neural crest- and placode-derived sensory neurons; neurotrophic activities were inhibited by neutralising antibodies for NGF and neurotrophin-4, respectively. High molecular isoforms of neurotrophins have been reported to occur in experimental colitis and in the inflamed gut of patients with Crohn's disease and ulcerative colitis, tissue sites rich in mast cells. The data suggest an important role for neurotrophins in the pathophysiology of inflammatory disease.

L3 ANSWER 16 OF 24 CAPLUS COPYRIGHT 2004 ACS on STN

1999:795994 Document No. 132:31744 Gene probes used for genetic profiling in healthcare screening and planning. Roberts, Gareth Wyn (Genostic Pharma Ltd., UK). PCT Int. Appl. WO 9964627 A2 19991216, 745 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-GB1780 19990604. PRIORITY: GB 1998-12099 19980606; GB 1998-13291 19980620; GB 1998-13611 19980624; GB 1998-13835 19980627; GB 1998-14110 19980701; GB 1998-14580 19980707; GB 1998-15438 19980716; GB 1998-15576 19980718; GB 1998-15574 19980718; GB 1998-16085 19980724; GB 1998-16086 19980724; GB 1998-16921 19980805; GB 1998-17097 19980807; GB 1998-17200 19980808; GB 1998-17632 19980814; GB 1998-17943 19980819.

AB There is considerable evidence that significant factor underlying the individual variability in response to disease, therapy and prognosis lies in a person's genetic make-up. There have been numerous examples relating that polymorphisms within a given gene can alter the functionality of the protein encoded by that gene thus leading to a variable physiol. response. In order to bring about the integration of genomics into medical practice and enable design and building of a technol. platform which will enable the everyday practice of mol. medicine a way must be invented for the DNA sequence data to be aligned with the identification of genes central to the induction, development, progression and outcome of disease or physiol. states of interest. According to the invention, the number of genes and their configurations (mutations and polymorphisms) needed to be identified in order to provide critical clin. information concerning individual prognosis is considerably less than the 100,000 thought to comprise the

human genome. The identification of the identity of the core group of genes enables the invention of a design for genetic profiling technologies which comprises of the identification of the core group of genes and their sequence variants required to provide a broad base of clin. prognostic information - "genostics". The "Genostic" profiling of patients and persons will radically enhance the ability of clinicians, healthcare professionals and other parties to plan and manage healthcare provision and the targeting of appropriate healthcare resources to those deemed most in need. The use of this invention could also lead to a host of new applications for such profiling technologies, such as identification of persons with particular work or environment related risk, selection of applicants for employment, training or specific opportunities or for the enhancing of the planning and organization of health services, education services and social services.

L3 ANSWER 17 OF 24 CAPLUS COPYRIGHT 2004 ACS on STN

1999:795993 Document No. 132:31743 Gene probes used for genetic profiling in healthcare screening and planning. Roberts, Gareth Wyn (Genostic Pharma Limited, UK). PCT Int. Appl. WO 9964626 A2 19991216, 149 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-GB1779 19990604. PRIORITY: GB 1998-12098 19980606; GB 1998-28289 19981223.

AB There is considerable evidence that significant factor underlying the individual variability in response to disease, therapy and prognosis lies in a person's genetic make-up. There have been numerous examples relating that polymorphisms within a given gene can alter the functionality of the protein encoded by that gene thus leading to a variable physiol. response. In order to bring about the integration of genomics into medical practice and enable design and building of a technol. platform which will enable the everyday practice of mol. medicine a way must be invented for the DNA sequence data to be aligned with the identification of genes central to the induction, development, progression and outcome of disease or physiol. states of interest. According to the invention, the number of genes and their configurations (mutations and polymorphisms) needed to be identified in order to provide critical clin. information concerning individual prognosis is considerably less than the 100,000 thought to comprise the human genome. The identification of the identity of the core group of genes enables the invention of a design for genetic profiling technologies.

L3 ANSWER 18 OF 24 CAPLUS COPYRIGHT 2004 ACS on STN

1999:764208 Document No. 132:10492 Chimeric molecules comprising an extracellular ligand-binding domain of a receptor and an **IgE** Fc or constant region, and their use in assay systems. Stahl, Neil; Karow, Margaret; Yancopoulos, George D. (Regeneron Pharmaceuticals, Inc., USA; The Procter & Gamble Co.). PCT Int. Appl. WO 9961630 A2 19991202, 55 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US11619 19990526. PRIORITY: US 1998-84697 19980526.

AB The present invention provides for a general, rapid, cell-based assay system that utilizes the unique features of the **IgE** high affinity receptor FcεRI and the rapid, characteristic degranulation phenotype exhibited by mast cells and basophils following

antigen binding to, and crosslinking of, monomeric **IgE** bound to the receptor on such cells. Identifying a ligand for a receptor comprises contacting a cell expressing a cell surface FcεRI with a chimeric polypeptide comprising an extracellular ligand-binding domain of a receptor and an **IgE** constant or Fc region, and and detecting or measuring ligand binding to the complex. The invention further provides for chimeric polypeptide mols., the nucleic acids encoding the chimeric polypeptide mols., and cell lines expressing the chimeric polypeptide mols. In particular, the chimeric polypeptide mols. comprise an extracellular ligand binding domain selected from the granulocyte colony-stimulating factor receptor, the muscle-specific kinase receptor, the bone morphogenic protein receptor, the leptin receptor, the ciliary **neurotrophic factor** receptor α, the gp130 receptor, and the erythropoietin receptor.

L3 ANSWER 19 OF 24 CAPLUS COPYRIGHT 2004 ACS on STN

1999:194265 Document No. 130:233822 Rin2, a novel inhibitor of Ras-mediated signaling and a cDNA encoding it. Tam, See-ying; Tsai, Mindy; Galli, Stephen J. (Beth Israel Deaconess Medical Center, USA). PCT Int. Appl. WO 9913079 A1 19990318, 102 pp. DESIGNATED STATES: W: AU, CA, JP, US, US; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1998-US19056 19980911. PRIORITY: US 1997-58520 19970911; US 1997-942819 19971002.

AB A novel gene, Rin2, that plays a role in regulating ras-mediated signal transduction is identified and characterized. The gene and gene product may be used in modulation of Ras-dependent signaling in the treatment of disease. Rin-2 function is induced mast cells in response to stimuli that activate them, such as activation of FcεRI. The results of antisense inhibition of rin2 gene expression suggest that the Rin2 gene product down-regulates responses to activating stimuli. The gene was identified by mRNA differential display in mast cells activated by **IgE** and antigens. The PCR product was used to probe a mouse mast cell cDNA library and BLAST anal. indicated that the gene product was a GTPase-binding protein. Partial cDNAs for the human equivalent of Rin-2 were also cloned.

L3 ANSWER 20 OF 24 CAPLUS COPYRIGHT 2004 ACS on STN

1999:693667 Document No. 132:22097 Cellular sources of enhanced brain-derived **neurotrophic factor** production in a mouse model of allergic inflammation. Braun, Armin; Lommatzsch, Marek; Mannsfeldt, Anne; Neuhaus-Steinmetz, Ulrich; Fischer, Axel; Schnoy, Norbert; Lewin, Gary R.; Renz, Harald (Institut fur Laboratoriumsmedizin und Pathobiochemie, Charite-Campus Virchow-Klinikum, and Max Delbruck Centrum, Humboldt Universitat, Berlin, Germany). American Journal of Respiratory Cell and Molecular Biology, 21(4), 537-546 (English) 1999. CODEN: AJRBEL. ISSN: 1044-1549. Publisher: American Lung Association.

AB The aim of this study was to investigate production and cellular sources of brain-derived **neurotrophic factor** (BDNF) production in allergic asthma. For this purpose a mouse model of chronic and severe ovalbumin (OVA)-induced airway inflammation was developed. Allergen-exposed mice developed elevated **IgE** titers; airway inflammation with influx of lymphocytes, monocytes, and eosinophils; and airway hyperresponsiveness. In addition to an influx of inflammatory cells, interleukin (IL)-4 and IL-5 production were enhanced, macrophages showed morphol. signs of activation, and airway epithelium was thickened and displayed a goblet-cell hyperplasia with a marked mucus production BDNF was detected using in situ hybridization and ELISA. Constitutive expression of BDNF mRNA was observed in the respiratory epithelium of sensitized and nonsensitized mouse lungs. In addition, BDNF mRNA was detected in airway inflammatory infiltrations and bronchoalveolar lavage fluid (BALF) cells of OVA-sensitized and aerosol-challenged mice. Highest BDNF protein levels were detected in BALF after long-term allergen aerosol exposure. Anal. of BDNF production by isolated lymphocyte subsets revealed T but not B cells as a cellular source of BDNF. In addition, activated alveolar macrophages were identified as BDNF-pos. cells. These data indicate that

in allergic airway inflammation BDNF production is upregulated and immune cells serve as a source of BDNF.

L3 ANSWER 21 OF 24 CAPLUS COPYRIGHT 2004 ACS on STN
1998:488694 Document No. 129:212045 Effects of nerve growth factor (NGF) and other fibroblast-derived growth factors on immature human mast cells (HMC-1). Welker, P.; Grabbe, J.; Grutzkau, A.; Henz, B. M. (Dep. Dermatology, Charite-Virchow Clinic, Humboldt-Univ., Berlin, Germany). Immunology, 94(3), 310-317 (English) 1998. CODEN: IMMUAM. ISSN: 0019-2805. Publisher: Blackwell Science Ltd..

AB The authors have previously shown that fibroblast and keratinocyte supernatants up-regulate expression of mast cell characteristics in the human immature mast cell line HMC-1. This effect could not be induced in HMC-1 cells by the well-known mast cell growth factor stem cell factor (SCF), probably due to mutations of the SCF receptor c-Kit in these cells. Here the authors report the effects of several known fibroblast- and keratinocyte-derived growth factors, namely nerve growth factor (NGF), basic fibroblast growth factor, platelet-derived growth factor and transforming growth factor-β, on mast cell differentiation, using HMC-1 cells as a model. NGF, at 0.1-50 ng/mL concns., caused a marked, dose-dependent up-regulation of tryptase, FcεRI and histamine within 10 days of culture, associated with an enhanced expression of mRNA for FcεRI and mast cell tryptase. On restriction anal., only mast cell β-tryptase, but not α-tryptase, could be demonstrated. Furthermore, the high-affinity NGF receptor (TrkA) was found at both the transcriptional and protein levels, while expression of the low-affinity NGF receptor was detectable at the mRNA level only. None of the other growth factors caused a significant alteration of the mast cell markers studied when added to HMC-1 cells at concns. known to be biol. active in other culture systems. Immature human mast cells are thus induced to assume a more mature phenotype in vitro in response to NGF, most probably via stimulation of the high-affinity NGF receptor expressed on these cells. Besides SCF, NGF should therefore be considered as an addnl. mast cell growth factor that contributes to human mast cell maturation at tissue sites.

L3 ANSWER 22 OF 24 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
1998:153861 Document No.: PREV199800153861. Brain-derived **neurotrophic factor** (BDNF) is upregulated in airway inflammations of allergen-sensitized Balb/c mice. Lommatzsch, M. [Reprint author]; Braun, A. [Reprint author]; Mannsfeldt, A.; Schnoy, N. [Reprint author]; Lewin, G.; Renz, H. [Reprint author]. Virchow Clinic, Humboldt Univ., Berlin, Germany. Journal of Allergy and Clinical Immunology, (Jan., 1998) Vol. 101, No. 1 PART 2, pp. S34-S35. print.
Meeting Info.: 54th Annual Meeting of the American Academy of Allergy, Asthma and Immunology. Washington, DC, USA. March 13-18, 1998. American Academy of Allergy, Asthma, and Immunology.
CODEN: JACIBY. ISSN: 0091-6749. Language: English.

L3 ANSWER 23 OF 24 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
97:767660 The Genuine Article (R) Number: YA324. Human mast cells express functional TrkA and are a source of nerve growth factor. Nilsson G (Reprint); ForsbergNilsson K; Xiang Z; Hallbook F; Nilsson K; Metcalfe D D . UNIV UPPSALA, DEPT PATHOL, S-75185 UPPSALA, SWEDEN (Reprint); NIAID, LAB ALLERG DIS, NIH, BETHESDA, MD 20892; NINCDS, MOL BIOL LAB, NIH, BETHESDA, MD 20892; UNIV UPPSALA, DEPT DEV NEUROSCI, UPPSALA, SWEDEN. EUROPEAN JOURNAL OF IMMUNOLOGY (SEP 1997) Vol. 27, No. 9, pp. 2295-2301. Publisher: VCH PUBLISHERS INC. 303 NW 12TH AVE, DEERFIELD BEACH, FL 33442-1788. ISSN: 0014-2980. Pub. country: SWEDEN; USA. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Mast cells are the principal effector cells in **IgE**-dependent hypersensitivity reactions. Despite reports that rodent mast cells proliferate in the presence of nerve growth factor (NGF), human mast cells reportedly do not respond to this factor. To determine if human mast cells express the NGF receptors, TrkA tyrosine receptor and the low affinity NGF

receptor (LNGFR), we first analyzed the mRNA expression by RT-PCR of TrkA and LNGFR in a human mast cell line (HMC-1) and in human mast cells cultured in the presence of stem cell factor. Both HMC-1 and cultured human mast cells were found to express TrkA but not LNGFR. TrkA protein was demonstrated by Western blot analysis of HMC-1 lysates. Using flow cytometric analysis and mast cell tryptase as a mast cell marker, both HMC-1 cells and cultured human mast cells were shown to coexpress tryptase and TrkA. Treatment of mast cells with NGF resulted in phosphorylation of TrkA on tyrosine residues as detected by immunoblotting with an antiphosphotyrosine antibody. Furthermore, NGF induced the immediate early gene c-fos in HMC-1 cells. HMC-1 cells and cultured human mast cells were also found to express NGF mRNA, and conditioned medium from HMC-1 cells stimulated neurite outgrowth from chicken embryonic sensory ganglia in culture. This effect was blocked by anti-NGF. Thus, mast cells express functional TrkA and synthesize NGF, suggesting a mechanism by which NGF may act as an autocrine factor for human mast cells, and by which mast cells and nerves may interact.

L3 ANSWER 24 OF 24 MEDLINE on STN DUPLICATE 2
96152742 Document Number: 96152742. PubMed ID: 8566063. Nerve growth-factor and anti-CD40 provide opposite signals for the production of **IgE** in interleukin-4-treated lymphocytes. Brodie C; Oshiba A; Renz H; Bradley K; Gelfand E W. (Department of Pediatrics, National Jewish Center for Immunology and Respiratory Medicine, Denver, CO 80206, USA.) EUROPEAN JOURNAL OF IMMUNOLOGY, (1996 Jan) 26 (1) 171-8. Journal code: 1273201. ISSN: 0014-2980. Pub. country: GERMANY: Germany, Federal Republic of. Language: English.

AB Nerve growth factor (NGF) is a well-known **neurotrophic factor** acting on both the peripheral and the central nervous systems. In addition, it has been shown to play a role in the function of the immune system through specific receptors. Both high-affinity and low-affinity NGF receptors (NGFR) are expressed on human B lymphocytes. The low-affinity NGFR has been shown to have structural homology with another specific B cell surface molecule, CD40, which plays an important role in **IgE** production. In view of the structural similarities of the p75 NGFR and CD40 we examined whether NGF may also be involved in the regulation of **IgE** production. We found that NGF and anti-CD40 exerted opposite effects on the induction of **IgE** by IL-4 in peripheral blood mononuclear cells. NGF inhibited the induction of **IgE** by IL-4 and this inhibition was not mediated through blocking of the induction of CD23 nor through inhibition of IL-4R expression. The inhibition of IL-4-dependent **IgE** production was observed on surface (s)**IgE**+ and sIgE-/sIgM+ B lymphocytes. Anti-CD40 on the other hand, exerted an enhancing effect on **IgE** production and its addition to IL-4 provided a signal that was resistant to the inhibitory effect of NGF. Antagonistic effects of NGF and IL-4 were also observed for other Ig isotypes since IL-4 prevented the increase in IgA and IgM production induced by NGF. These data indicate that although NGFR and CD40 belong to the same receptor superfamily and exert similar proliferative effects on B lymphocytes, they interact differently with IL-4 in the regulation of **IgE** production.

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L6 ANSWER 1 OF 7 MEDLINE on STN DUPLICATE 1

2003125531 Document Number: 22526365. PubMed ID: 12639901. Novel neurotrophin-1/B cell-stimulating factor-3 (cardiotrophin-like cytokine) stimulates corticotroph function via a signal transducer and activator of transcription-dependent mechanism negatively regulated by suppressor of cytokine signaling-3. Auernhammer Christoph J; Isele Nicola B; Kopp Florian B; Spoettl Gerald; Cengic Neziha; Weber Matthias M; **Senaldi Giorgio**; Engelhardt Dieter. (Department of Internal Medicine II, Klinikum Grosshadern, Ludwig-Maximilians-Universitat, Munich 81366, Germany.. christoph.auernhammer@med2.med.uni-muenchen.de) . ENDOCRINOLOGY, (2003 Apr) 144 (4) 1202-10. Journal code: 0375040. ISSN: 0013-7227. Pub. country: United States. Language: English.

AB Novel neurotrophin-1/B cell-stimulating factor-3 (**NNT-1** /BSF-3) is a recently cloned gp130 cytokine, acting through the tripartite ciliary neurotrophic factor receptor (CNTFR) alpha/leukemia inhibitory factor receptor (LIFR)/gp130 receptor complex. The aim of the current study was to investigate the role of **NNT-1**/BSF-3 in corticotroph cell function and further characterize **NNT-1**/BSF-3 signaling pathways. Using RT-PCR, expression of ciliary neurotrophic factor receptor alpha, leukemia inhibitory factor receptor, and gp130 could be demonstrated in mRNA derived from murine corticotroph AtT-20 cells and murine pituitary tissue. Incubation of AtT-20 cells with 10 ng/ml recombinant human **NNT-1**/BSF-3 rapidly induced tyrosine-phosphorylation of signal transducer and activator of transcription (STAT)3 and STAT1 at 5 and 10 min. Proopiomelanocortin promoter activity and suppressor of cytokine signaling (SOCS)-3 promoter activity were significantly stimulated by **NNT-1**/BSF-3 4.0 +/- 0.3- and 5.9 +/- 0.2-fold, respectively. In comparison with untreated control, **NNT-1**/BSF-3 significantly stimulated ACTH secretion at 24 and 48 h 1.7 +/- 0.2-fold and 1.5 +/- 0.1-fold above baseline. In comparison with mock-transfected cells, stable overexpression of SOCS-3 in AtT-20 cells abolished **NNT-1**/BSF-3-induced STAT1 and STAT3 phosphorylation and almost completely inhibited STAT-dependent proopiomelanocortin promoter and SOCS-3 promoter activities. In addition, **NNT-1** /BSF-3-induced ACTH secretion at 48 h was significantly attenuated by SOCS-3 overexpression. In summary, we have shown that **NNT-1**/BSF-3 is a modulator of corticotroph cell function, which is negatively regulated by SOCS-3. Our data indicate that the activation of the Jak-STAT cascade is essential for corticotroph **NNT-1** /BSF-3 signaling. Further studies will have to investigate the possible in vivo role of **NNT-1**/BSF-3 as a neuroimmunoendocrine modulator of hypothalamus-pituitary-adrenal axis stress response.

L6 ANSWER 2 OF 7 MEDLINE on STN DUPLICATE 2

2003595493. PubMed ID: 14632778. Functional significance of novel neurotrophin-1/B cell-stimulating factor-3 (cardiotrophin-like cytokine) for human myeloma cell growth and survival. Burger Renate; Bakker Frank; Guenther Andreas; Baum Wolfgang; Schmidt-Arras Dirk; Hideshima Teru; Tai Yu-Tzu; Shringarpure Reshma; Catley Laurence; **Senaldi Giorgio**; Gramatzki Martin; Anderson Kenneth C. (Jerome Lipper Multiple Myeloma Center, Department of Medical Oncology, Dana-Farber Cancer Institute, Boston, MA 02115, USA.) British journal of haematology, (2003 Dec) 123 (5) 869-78. Journal code: 0372544. ISSN: 0007-1048. Pub. country: England: United Kingdom. Language: English.

AB Cytokines of the gp130 family, particularly interleukin 6 (IL-6), play a central role in the growth and survival of malignant plasma cells. Recently, novel neurotrophin-1 (**NNT-1**)/B cell-stimulating factor-3 (BSF-3), also reported as cardiotrophin-like cytokine (CLC), was identified as a cytokine belonging to the gp130 family. BSF-3, similar to IL-6, exerts regulatory effects on normal B cell functions, but its functional significance in haematological malignancies has not been defined. The purpose of this study was to evaluate the biological effects and signalling pathways that are induced by BSF-3 in malignant plasma cells. Recombinant human BSF-3 was found to

have growth stimulatory activity on plasmacytoma cell lines and primary tumour cells. In addition, BSF-3 was able to protect from Dexamethasone (Dex)-induced apoptosis. BSF-3 stimulated cell growth could not be inhibited by neutralizing anti-IL-6 or anti-IL-6 receptor antibodies, but was abrogated by anti-gp130 antibodies. In INA-6.Tu11 cells, a subline of the IL-6-dependent human plasma cell line INA-6 expressing gp130 and the receptor for leukaemia inhibitory factor (LIF), stimulation with BSF-3 induced tyrosine phosphorylation of signal transducer and activator of transcription 3 (STAT3). AG490, an inhibitor of Janus kinases, decreased BSF-3 induced cell growth in a dose-dependent manner. This correlated with a reduction of STAT3 phosphorylation levels, while p44/42 mitogen-activated protein kinase (MAPK) phosphorylation was not affected. In conclusion, BSF-3 is a novel myeloma growth and survival factor with a potential role in the pathophysiology of the disease.

L6 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN
2002:157624 Document No. 136:215409 Anti-novel neurotrophic factor 1 (**NNT-1**) antibodies and soluble **NNT-1** receptor for treating IgE-related disease. **Senaldi, Giorgio** (Amgen Inc., USA). PCT Int. Appl. WO 2002015977 A2 20020228, 63 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US25906 20010817. PRIORITY: US 2000-PV226436 20000818; US 2001-931704 20010816.

AB Disclosed are novel methods and compns. for diagnosing and treating IgE-related diseases using **NNT-1** inhibitors. The **NNT-1** inhibitors include antagonistic anti-**NNT-1** antibodies, chimeric or humanized antibodies, and CDR-grafted antibodies or fragments, as well as soluble **NNT-1** receptor. The IgE-related diseases include allergy, allergic rhinitis, eczema, dermatitis, pollinosis, asthma, and others. In one embodiment, the present invention relates to a method of treating IgE-related diseases using a selective binding agent to **NNT-1**. In another embodiment, the present invention relates to a method of treating IgE-related diseases using an **NNT-1** expression modulator. Methods of modulating IgE levels, and of diagnosing, preventing and/or treating certain types of allergic diseases using **NNT-1** inhibitors are also disclosed.

L6 ANSWER 4 OF 7 MEDLINE on STN DUPLICATE 3
2002286930 Document Number: 22018151. PubMed ID: 12023368. Regulatory effects of novel neurotrophin-1/b cell-stimulating factor-3 (cardiotrophin-like cytokine) on B cell function. **Senaldi Giorgio** ; Stolina Marina; Guo Jane; Faggioni Raffaella; McCabe Susan; Kaufman Stephen A; Van Gwyneth; Xu Weilong; Fletcher Frederick A; Boone Thomas; Chang Ming-Shi; Sarmiento Ulla; Cattley Russell C. (Amgen, Inc., Thousand Oaks, CA 91320, USA.. gsenaldi@amgen.com) . JOURNAL OF IMMUNOLOGY, (2002 Jun 1) 168 (11) 5690-8. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB We describe regulatory effects that a novel neurotrophin-1/B cell-stimulating factor-3 (**NNT-1**/BSF-3; also reported as cardiotrophin-like cytokine) has on B cell function. **NNT-1**/BSF-3 stimulates B cell proliferation and Ig production in vitro. **NNT-1**/BSF-3-transgenic mice, engineered to express **NNT-1**/BSF-3 in the liver under control of the apolipoprotein E promoter, show B cell hyperplasia with particular expansion of the mature follicular B cell subset in the spleen and the prominent presence of plasma cells. **NNT-1** /BSF-3-transgenic mice show high serum levels of IgM, IgE, IgG2b, IgG3,

anti-dsDNA Abs, and serum amyloid A. **NNT-1**
/BSF-3-transgenic mice also show non-amyloid mesangial deposits that contain IgM, IgG, and C3 and are characterized by a distinctive ultrastructure similar to that of immunotactoid glomerulopathy. **NNT-1**/BSF-3-transgenic mice produce high amounts of Ag-specific IgM, IgA, and IgE and low amounts of IgG2a and IgG3. Normal mice treated with **NNT-1**/BSF-3 also produce high amounts of Ag-specific IgE. **NNT-1**/BSF-3 regulates immunity by stimulating B cell function and Ab production, with preference for Th2 over Th1 Ig types.

L6 ANSWER 5 OF 7 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
2003:51944 Document No.: PREV200300051944. Novel neurotrophin-1/B cell stimulating factor-3 (**NNT-1**/BSF-3) stimulates osteoblastic cell activities in vitro including bone formation and IL-6 production. Stolina, Marina [Reprint Author]; Grisanti, Mario [Reprint Author]; Shalhoub, Victoria [Reprint Author]; **Senaldi, Giorgio** [Reprint Author]. Amgen, Inc., Thousand Oaks, CA, USA. Journal of Interferon and Cytokine Research, (2002) Vol. 22, No. Supplement 1, pp. S-98-S-99. print.
Meeting Info.: Joint Meeting of the International Society for Interferon and Cytokine Research, the International Cytokine Society, the Society for Leukocyte Biology, and the European Cytokine Society on Cytokines and Interferons. Turin, Italy. October 06-10, 2002. International Society for Interferon and Cytokine Research.
ISSN: 1079-9907 (ISSN print). Language: English.

L6 ANSWER 6 OF 7 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
2002:186711 Document No.: PREV200200186711. B-cell stimulating factor-3/novel neurotrophin-1: A novel myeloma cell growth factor of the GP130-family. Burger, Renate [Reprint author]; Bakker, Frank [Reprint author]; Guenther, Andreas [Reprint author]; Baum, Wolfgang [Reprint author]; **Senaldi, Giorgio**; Gramatzki, Martin [Reprint author]. Division of Hematology/Oncology, Department of Medicine III, University of Erlangen-Nuernberg, Erlangen, Germany. Blood, (November 16, 2001) Vol. 98, No. 11 Part 1, pp. 373a. print.
Meeting Info.: 43rd Annual Meeting of the American Society of Hematology, Part 1. Orlando, Florida, USA. December 07-11, 2001. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971. Language: English.
AB Novel neurotrophin-1 (**NNT-1**)/B cell-stimulating factor-3 (BSF-3), also named cardiotrophin-like cytokine (CLC), was recently cloned and characterized to belong to the class of interleukin (IL)-6-type cytokines. The members of this family, namely IL-6, IL-11, leukemia inhibitory factor (LIF), oncostatin M (OSM), ciliary neurotrophic factor (CNTF) and cardiotrophin-1 (CT-1), all use the gp130 signaling subunit as a part of their receptor complexes. Along with gp130, the cellular receptor for BSF-3 also includes the LIF receptor (LIFR) beta-chain. BSF-3, similar to IL-6, possesses B celL-stimulating capability. Since IL-6 is a major growth factor for malignant plasma cells, BSF-3 could also play a role in multiple myeloma. We used a gp130/LIFR expressing subline of the IL-6-dependent human plasma cell line INA-6 to evaluate BSF-3 activity and to characterize the intracellular signaling pathways that are induced by BSF-3. Growth of the human plasmacytoma cell line INA-6/Tu11 is dependent on IL-6 and the cells also respond to other cytokines of the gp130-family. Stimulation of Tu11 cells with human recombinant BSF-3 significantly induced cell proliferation as measured by (3H)thymidine uptake. BSF-3 induced proliferation was almost completely blocked by anti-gp130 monoclonal antibodies. Interestingly, an anti-gp130 antibody that specifically neutralizes CNTF activity, significantly reduced BSF-3 induced DNA synthesis. As with the other gp130-cytokines, the tyrosine kinase inhibitor tyrphostin AG490 blocked BSF-3 induced proliferation in a dose-dependent manner indicating the involvement of Jak kinases in signal transduction. It could be shown by immunoblotting that STAT3 is phosphorylated on tyrosine residues upon

stimulation with BSF-3. For the first time, it can be demonstrated that BSF-3, a novel member of the gp130-family of cytokines, promotes plasmacytoma cell growth and activates the Jak/STAT signaling pathway. The results also indicate that the physiological CNTF receptor may participate in BSF-3 binding on human plasma cells. BSF-3 is strongly expressed in secondary lymph organs and in bone tissue, and may play a role in the pathophysiology of multiple myeloma, thereby acting in a paracrine or even autocrine manner.

L6 ANSWER 7 OF 7 MEDLINE on STN DUPLICATE 4
1999432254 Document Number: 99432254. PubMed ID: 10500198. Novel neurotrophin-1/B cell-stimulating factor-3: a cytokine of the IL-6 family. **Senaldi G**; Varnum B C; Sarmiento U; Starnes C; Lile J; Scully S; Guo J; Elliott G; McNinch J; Shaklee C L; Freeman D; Manu F; Simonet W S; Boone T; Chang M S. (Amgen Inc., Thousand Oaks, CA 91320, USA.. gsnaldi@amgen.com) . PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1999 Sep 28) 96 (20) 11458-63. Journal code: 7505876. ISSN: 0027-8424. Pub. country: United States. Language: English.

AB We have identified a cytokine of the IL-6 family and named it novel neurotrophin-1/B cell-stimulating factor-3 (**NNT-1** /BSF-3). **NNT-1**/BSF-3 cDNA was cloned from activated Jurkat human T cell lymphoma cells. Its sequence predicts a 225-aa protein with a 27-aa signal peptide, a molecular mass of 22 kDa in mature form, and the highest homology to cardiotrophin-1 and ciliary neurotrophic factor. The gene for **NNT-1**/BSF-3 is on chromosome 11q13. A murine equivalent to **NNT-1**/BSF-3 also was identified, which shows 96% homology to human **NNT-1** /BSF-3. **NNT-1**/BSF-3 mRNA is found mainly in lymph nodes and spleen. **NNT-1**/BSF-3 induces tyrosine phosphorylation of glycoprotein 130 (gp130), leukemia inhibitory factor receptor beta, and signal transducer and activator of transcription 3 in the SK-N-MC human neuroblastoma cells. **NNT-1**/BSF-3 shows activities typical of IL-6 family members. In vitro, it supports the survival of chicken embryo motor and sympathetic neurons. In mice, it induces serum amyloid A, potentiates the induction by IL-1 of corticosterone and IL-6, and causes body weight loss and B cell hyperplasia with serum IgG and IgM increase. **NNT-1** /BSF-3 is a gp130 activator with B-cell stimulating capability.

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=> s "B cell stimulating factor 3" and IgE production
   3 FILES SEARCHED...
L7            0 "B CELL STIMULATING FACTOR 3" AND IGE PRODUCTION

=> d his

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     FILE 'MEDLINE, EMBASE, BIOSIS, SCISEARCH, CAPLUS' ENTERED AT 11:18:12 ON
     12 FEB 2004
L1         49093 S NEUROTROPHIC FACTOR
L2            32 S L1 AND IGE
L3            24 DUP REMOVE L2 (8 DUPLICATES REMOVED)
L4           458 S (SENALDI G?/AU)
L5            23 S L4 AND "NNT-1"
L6             7 DUP REMOVE L5 (16 DUPLICATES REMOVED)
L7             0 S "B CELL STIMULATING FACTOR 3" AND IGE PRODUCTION

=> s l5 and IgE
L8             6 L5 AND IGE

=> dup remove l8
PROCESSING COMPLETED FOR L8
L9             2 DUP REMOVE L8 (4 DUPLICATES REMOVED)
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L9 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN
2002:157624 Document No. 136:215409 Anti-novel neurotrophic factor 1 (**NNT-1**) antibodies and soluble **NNT-1** receptor for treating **IgE**-related disease. **Senaldi, Giorgio** (Amgen Inc., USA). PCT Int. Appl. WO 2002015977 A2 20020228, 63 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US25906 20010817. PRIORITY: US 2000-PV226436 20000818; US 2001-931704 20010816.

AB Disclosed are novel methods and compns. for diagnosing and treating **IgE**-related diseases using **NNT-1** inhibitors. The **NNT-1** inhibitors include antagonistic anti-**NNT-1** antibodies, chimeric or humanized antibodies, and CDR-grafted antibodies or fragments, as well as soluble **NNT-1** receptor. The **IgE**-related diseases include allergy, allergic rhinitis, eczema, dermatitis, pollinosis, asthma, and others. In one embodiment, the present invention relates to a method of treating **IgE**-related diseases using a selective binding agent to **NNT-1**. In another embodiment, the present invention relates to a method of treating **IgE**-related diseases using an **NNT-1** expression modulator. Methods of modulating **IgE** levels, and of diagnosing, preventing and/or treating certain types of allergic diseases using **NNT-1** inhibitors are also disclosed.

L9 ANSWER 2 OF 2 MEDLINE on STN DUPLICATE 1
2002286930 Document Number: 22018151. PubMed ID: 12023368. Regulatory effects of novel neurotrophin-1/b cell-stimulating factor-3 (cardiotrophin-like cytokine) on B cell function. **Senaldi Giorgio** ; Stolina Marina; Guo Jane; Faggioni Raffaella; McCabe Susan; Kaufman Stephen A; Van Gwyneth; Xu Weilong; Fletcher Frederick A; Boone Thomas; Chang Ming-Shi; Sarmiento Ulla; Cattley Russell C. (Amgen, Inc., Thousand Oaks, CA 91320, USA.. gsenaldi@amgen.com) . JOURNAL OF IMMUNOLOGY, (2002 Jun 1) 168 (11) 5690-8. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB We describe regulatory effects that a novel neurotrophin-1/B cell-stimulating factor-3 (**NNT-1**/BSF-3; also reported as cardiotrophin-like cytokine) has on B cell function. **NNT-1**/BSF-3 stimulates B cell proliferation and Ig production in vitro. **NNT-1**/BSF-3-transgenic mice, engineered to express **NNT-1**/BSF-3 in the liver under control of the apolipoprotein E promoter, show B cell hyperplasia with particular expansion of the mature follicular B cell subset in the spleen and the prominent presence of plasma cells. **NNT-1** /BSF-3-transgenic mice show high serum levels of IgM, **IgE**, IgG2b, IgG3, anti-dsDNA Abs, and serum amyloid A. **NNT-1** /BSF-3-transgenic mice also show non-amyloid mesangial deposits that contain IgM, IgG, and C3 and are characterized by a distinctive ultrastructure similar to that of immunotactoid glomerulopathy. **NNT-1**/BSF-3-transgenic mice produce high amounts of Ag-specific IgM, IgA, and **IgE** and low amounts of IgG2a and IgG3. Normal mice treated with **NNT-1**/BSF-3 also produce high amounts of Ag-specific **IgE**. **NNT-1**/BSF-3 regulates immunity by stimulating B cell function and Ab production, with preference for Th2 over Th1 Ig types.

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	108.85	109.06

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-15.25	-15.25

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